10/578763

DESCRIPTION IAP20 Rec'd PCT/PTO 05 MAY 2006

CONTAINER FOR PACKING REAGENT

TECHNICAL FIELD

The present invention relates to a container for packing a reagent (hereunder, reagent container), and relates particularly to a reagent container comprising one or more liquid-containing units for containing a reagent.

BACKGROUND ART

When capturing, extracting, concentrating, testing, and analyzing substances contained in a container, such as genetic material like DNA, immunogenic substances, proteins, various biological substances, microorganisms such as bacteria, and viruses, an operation was required in which the contents of the container are heated or cooled in order to promote a reaction with a reagent contained in the container, or to break down the cell membrane, or to keep at a suitable temperature in order to preserve the substance in the container. For this purpose, a heating or cooling thermostatic unit (Japanese Unexamined Patent Publication No. Hei 13-074750, Japanese Unexamined Patent Publication No. 2002-214091, and FIG. 6 of WO01/53839 A1, for example), or a temperature control unit was required (Japanese Unexamined Patent Publication No. Hei 14-010777), and each liquid-containing unit had to be inserted into or installed in the thermostatic unit and its temperature controlled by heating or cooling, to preserve its contents or promote a reaction. To achieve heating or cooling in this manner, the thermostatic unit required an aluminum block, a Peltier element, a fan, fins, and the like, as well as a power source to drive them.

Incidentally, in recent years, given the reality of new diseases caused by new and unknown varieties of bacteria and viruses, the use of biochemical weapons, and the threat of bio-terrorism, there is a growing need for the analysis of viruses and the like to be performed quickly *in situ* in such locations as a battlefield, a region where a disease originated, or the site of a terrorist attack. In such an event, depending on the substance being tested or analyzed and the nature of the test or analysis, it is necessary to maintain the substance at a temperature higher or lower than ambient or room temperature over a long time, in order to break down the cell membrane or promote an incubation or other type of reaction. However, there has been a disadvantage in that heating or cooling to a temperature higher or lower than ambient or room temperature and maintaining that temperature over a long time using a heating device or cooling device comprising an aluminum block requires a larger electric capacity than can be provided by a battery source.

Furthermore, another disadvantage is that carrying around heating or cooling equipment comprising an aluminum block or a generator, places a burden on the user. Yet another disadvantage is that because such devices are expensive and must be reused, they must be sterilized after each use to prevent contamination.

A problem to be solved by the present invention is that heating and cooling over long periods of time must be performed using a generator, because a battery source is inadequate for the purpose.

Consequently, a first object of the present invention is to provide a portable reagent container by which heating or cooling can be maintained over a long time, and also highly accurate temperature control can be performed.

A second object is to provide an easily portable reagent container that enables a user to efficiently capture, extract, concentrate, test, and analyze substances such as genetic

material like DNA, immunogenic substances, proteins, various endobiotic substances, microorganisms such as bacteria, and viruses.

A third object is to provide a reagent container whereby a pathogen or the like causative of an occurring disease, or a biochemical weapon used in a battlefield or in a bioterrorist attack, can be easily, quickly and smoothly specified *in situ*.

A fourth object is to provide a disposable reagent container which can be manufactured at low cost, and need not be reused together with the thermostatic unit.

DISCLOSURE OF THE INVENTION

Principally, a first aspect of the invention is a reagent container comprising one or more liquid-containing units for containing a reagent, and a thermostat container provided so as to surround at least one of the liquid-containing units, wherein a heating agent or a cooling agent for heating or cooling the liquid-containing unit is provided inside the thermostat container, but outside the liquid-containing unit surrounded by the thermostat container.

Here, a "reagent" refers to the reagent required for the process performed using the container, and is typically a liquid. Examples include a reagent in which oligonucleotide groups covering a variety of base sequences are each immobilized to magnetic particles, and the magnetic particles are labeled with a fluorescent substance, and suspended in a liquid, an enzyme that promotes a hybridization reaction with the target genetic material, and a reagent, for example a chaotropic solution, which breaks down the cell membrane and extracts DNA or RNA or the like.

When there is a plurality of liquid-containing units, preferably the liquid-containing units are arranged in a row in the form of a cartridge or microplate. This

has an advantage in that a plurality of reagents can be stored in a compact and associative manner, improving ease of use. On this occasion, the liquid-containing unit surrounded by the thermostat container is preferably isolated from the other liquid-containing units, so that the heating or cooling does not affect the other liquid-containing units.

"Surrounding the liquid-containing unit" can mean surrounding the outside surface of the liquid-containing unit but not the opening, and can also mean surrounding the liquid-containing unit including all or part of the opening. A "thermostat container" has the function of insulating or reducing the transfer of heat in order to maintain the heating or cooling effect of the heating agent or cooling agent. For this reason, the thermostat container is formed from an insulating material, or given an insulating construction. The thermostat container may be in the form of a container which houses the liquid-containing unit and has a lid covering the top of the liquid-containing unit but not the opening, or in the form of a box in which one or more holes into which the liquid-containing units can be inserted are provided.

Because the thermostat container "surrounds at least one of the liquid-containing units", this includes a case where a plurality of liquid-containing units are collectively surrounded by a single thermostat container, a case where a plurality of liquid-containing units are each surrounded individually by a thermostat container, and any combination thereof. In this case, the temperature of each thermostat container may be the same or may differ.

A "heating agent" is a substance for maintaining a temperature higher than room or ambient temperature, and a "cooling agent" is a material for maintaining a temperature lower than room or ambient temperature. An example of a heating agent includes a mixture of iron powder, activated carbon, salt, water, and a water-retaining substance. This heating

agent generates heat by bringing about a chemical reaction between the iron powder and oxygen, and the water-retaining substance retains water. Iron powder is used to obtain the greatest possible surface area in contact with the air to promote the reaction, and a salt, such as table salt, is used to accelerate the reaction. The activated carbon is used as a catalyst that promotes oxidation. Examples of the water-retaining substance include sawdust, vermiculite, and diatomaceous earth. Alternatively, a small amount of an igniting agent can be used to start a combustion reaction of a self-burning heat generator comprising an oxide and a metal powder.

In one example of a cooling agent, an aperture section formed from a porous material such as a biscuit is provided over all or part of the thermostat member, which contains water, an easily vaporized gas containing alcohol, or a volatile gas. In another example, a water-absorbing resin is used as the cooling agent, and an aperture section or mouth section through which water can be introduced is provided. In this case, the cooling effect is enhanced by pre-cooling the water-absorbing resin having absorbed the water. Here, a water-absorbing resin is a high polymer which, on contact with water, absorbs the water, swells, and gelatinizes all the water. Classifications of water-absorbing resins include starches, carboxymethyl celluloses, polyacrylates, and povals. Alternatively, a cooling agent in the form of a liquefied cooling gas can be sprayed using a cooling spray onto the outer surface or exterior of the liquid-containing unit when the device is in use. The liquefied cooling gas is preferably nonflammable.

Furthermore, the container may be formed from an inorganic material such as glass or a metal such as aluminum, or a synthetic resin such as acrylic, polyethylene, polystyrene, or polypropylene. If the thermostat container will be heated, the material is preferably heat resistant. Moreover, for example, when performing cooling, a porous material like an

unglazed ceramic is used. Furthermore, the thermostat container is preferably made of a material or a construction with high thermal insulation effectiveness which insulates or reduces the transfer of heat between the container and the outside, so that the heat of reaction inside the container is efficiently transferred, which aids in the adjustment of the reagent temperature.

In comprising a thermostat container capable of accommodating a heating agent or a cooling agent, the reagent container according to the first aspect of the invention has an advantage in terms of heating and cooling, in that by placing a reagent which must be maintained at a predetermined temperature by heating or cooling in a liquid-containing unit where a thermostat container is provided, the reagent placed in the liquid-containing unit can be maintained at a temperature different from room or ambient temperature without requiring a complicated thermostatic device and without depending on a battery source or a generator. Furthermore, another advantage is that a reagent container can be provided which has a simple construction and can be manufactured at low cost, and which is disposable together with the thermostat container. Yet another advantage is that the reagent container is small and lightweight and therefore portable and able to be carried to any location, enabling quick and smooth use in such locations as the site of a disease outbreak, a battlefield, or the site of a terrorist attack.

In addition, the need for power consumption is eliminated by performing heat generation and absorption primarily through chemical changes or chemical reactions, and providing insulation from heat in the form of the surrounding thermostat container. Accordingly, electric power can be used for precise temperature control only, which reduces the overall power consumption, and enables precise temperature control to be performed using a portable battery source. In particular, when the anticipated rapid improvement in

battery performance, and the future commercialization of fuel cells are realized, then by incorporating these developments the present invention can provide a device capable of operating for increasingly long periods of time.

A second aspect of the invention is a reagent container in which the thermostat container comprises an aperture section and/or a mouth section which enables the transfer of a substance such as a gas between the inside of the thermostat container and the outside. The aperture section is a gap or gaps through which a substance such as a gas can enter or leave. For example when the thermostat container contains the aforementioned heating agent that uses iron powder, the aperture section is a ventilation hole or holes through which air is introduced, and may be holes in a breathable filter or a porous material which may not necessarily be visible to the naked eye. For example, in a case where the thermostat container has a porous construction and makes use of the heat of vaporization lost when the liquid absorbed by the surface of the porous material evaporates, the aperture section corresponds to the part of a material with the porous construction. In this case, the liquid is the cooling agent, and the large number of minute pores invisible to the naked eye correspond to the aperture section. Furthermore, in a case where, for example, a liquefied cooling gas as the cooling agent is sprayed by a cooling spray directly onto the outer surface of a liquid-containing unit surrounded by the box-shaped thermostat container, the apertures provided in the thermostat container so that the liquefied cooling gas from the cooling spray can be sprayed onto the liquid-containing unit, correspond to the aperture section.

The mouth section is used while it is closed by a lid or the liquid-containing unit or the like during heating or cooling. In this respect, the mouth section differs from the aperture section which is used while it is closed by a lid or a film during heating or cooling.

An aperture section may also be provided in the lid or the like in the mouth section. The mouth section is used to install the liquid-containing unit, or to supply the cooling agent or heating agent as described later. The lid or the liquid-containing unit may be removable from the mouth section, of may be fixed in place.

In a reagent container according to the second aspect of the invention, the thermostat container comprises an aperture section and/or a mouth section which enables the transfer of a substance such as a gas between the inside of the thermostat container and the outside. Accordingly, heating or cooling can be maintained through a chemical reaction with an external substance induced by introducing the external substance such as air or a liquefied cooling gas into the thermostat container, instead of through a chemical reaction between substances inside the thermostat container induced by applying a physical shock to the container. Accordingly, this aspect of the invention has an advantage in that there is no need to apply a physical shock, and heating or cooling can be initiated reliably by introducing the external substance.

A third aspect of the invention is a reagent container in which the thermostat container is secured to the liquid-containing unit surrounded by the thermostat container.

The liquid-containing unit may be secured to the reagent container, or may be removable from the reagent container.

In a reagent container according to the third aspect of the invention, the thermostat container is secured to the liquid-containing unit surrounded by the thermostat container. Accordingly, this aspect of the invention has an advantage in that tasks such as assembling the container by inserting the liquid-containing unit into the thermostat container or placing the heating agent or cooling agent into the thermostat container during use are not required, which improves ease of use even further.

A fourth aspect of the invention is a reagent container in which the thermostat container is removable from the liquid-containing unit surrounded by the thermostat container.

In a reagent container according to the fourth aspect of the invention, the thermostat container is provided in a removable manner with respect to the liquid-containing unit to be surrounded by the thermostat container. Accordingly, if the container is bulky when the liquid-containing unit is installed in the thermostat container, the thermostat container and the liquid-containing unit can be assembled only when the container of the invention is in use, and the liquid-containing unit can be removed from the thermostat container during transport to improve portability. Furthermore, this aspect of the invention has an advantage in that because the thermostat container and the liquid-containing unit are provided separately, efficiency of use can be improved by sharing one thermostat container between the liquid-containing units in a plurality of reagent containers.

A fifth aspect of the invention is a reagent container in which the cooling agent or heating agent is supplied from outside the thermostat container to the inside through the aperture section and/or mouth section in the thermostat container.

With this aspect of the present invention, the cooling agent or heating agent is supplied through the aperture section or the mouth section. In this case, the aperture section or mouth section is formed in a shape and size through which the cooling agent or heating agent can be supplied easily.

In a reagent container according to the fifth aspect of the invention, the heating agent or cooling agent is supplied to the thermostat container from the outside through the aperture section or the mouth section. Accordingly, there is no need to place the heating

agent or cooling agent inside the thermostat container in advance, which further simplifies the construction and lowers manufacturing costs. In addition, another advantage of this aspect of the invention is that because the heating agent or cooling agent can be added through the aperture section, or through the mouth section of a removable lid when one is provided, heating or cooling can be continued for a long period of time.

A sixth aspect of the invention is a reagent container in which all or some of the liquid-containing units contain a predetermined reagent, and the openings of at least those liquid-containing units that contain the reagent are sealed with a peelable or perforable sealing film. Here, the "sealing film" is formed, for example, from cellulose, aluminum foil, or vinyl.

Because in a reagent container according to the sixth aspect of the invention the openings of all or some of the liquid-containing units are respectively covered by a peelable sealing film, this aspect of the invention has an advantage in that the required reagents contained in the liquid-containing units can be used by simply peeling or perforating the sealing film, enabling processes to be performed quickly.

A seventh aspect of the invention is a reagent container in which the aperture section is sealed by a peelable or perforable sealing film. Here, the reason the aperture section is covered with a sealing film is to block the entry and exit of gases and the like and prevent heating or cooling from starting. By peeling the sealing film away from the aperture section, or perforating the film, the heating agent can be placed in contact with air or the like, the cooling agent can be introduced, or the cooling agent can be vaporized, thereby initiating heating or cooling.

Moreover, the method of initiating the heating or cooling is not restricted to this case, and heating or cooling may be initiated, for example, by spraying a liquefied cooling

gas onto the liquid-containing unit by way of a cooling spray, by using a spark produced by an ignition mechanism, or by providing a pouch containing water inside the thermostat container and breaking the pouch (Japanese Unexamined Patent Publication No. Hei 5 - 010526).

A seventh aspect of the invention is a reagent container in which the plurality of liquid-containing units are arranged in a straight line in cartridge or microplate form.

The reagent container according to the seventh aspect of the invention has an advantage in that because a sealing film is provided to cover the aperture section, and thermostatic processing of heating or cooling can be performed by simply peeling away or perforating the sealing film, the invention can be used quickly and efficiently. According to the sixth aspect and the seventh aspect of the invention, reagents can be used easily by peeling away or perforating the sealing film, and the inside of the liquid-containing unit can be heated or cooled easily at the same time.

An eighth aspect of the invention is a reagent container in which the reagent container comprises a base section, and the liquid-containing units and the thermostat container are provided on the base section so that the openings and/or aperture sections of the liquid-containing units are located at the base section.

With the reagent container according to the eighth aspect of the invention, the liquid-containing units are provided so that the openings and/or aperture sections of the liquid-containing units are located at the base section, and consequently the openings and/or aperture sections can be sealed by one sheet of film, which provides an advantage in that the reagents can be used easily and thermostatic processing can be performed by simply peeling or perforating the film.

A ninth aspect of the invention is a reagent container in which the reagent container

comprises a plurality of thermostat containers, and each thermostat container is set up to maintain a different temperature.

For example, one or some thermostat containers may be for heating, and one or some for cooling. Alternatively, either for heating or cooling, thermostat containers which maintain different temperatures can be provided by appropriately selecting a heating agent or a cooling agent. In this case, preferably the thermostat containers are identifiable by way of coloring, text, symbols, or graphics or the like, so that thermostat containers with different temperatures can be distinguished.

With the reagent container according to the ninth aspect of the invention, because a plurality of thermostat containers are provided which can each be set up to maintain a different temperature, and consequently one liquid-containing unit can be set to a variety of temperatures not by performing control to change the temperature but by transferring substances, this aspect of the invention has an advantage in that a temperature changing apparatus is not required, which enables the size of the device to be reduced. Furthermore, another advantage is that processes that require a variety of temperature control can be performed efficiently using just one reagent container.

A tenth aspect of the invention is a reagent container in which a temperature-sensing element having a temperature-sensitive substance which senses the temperature of the thermostat container and visually indicates a change in temperature, is provided on the plurality of thermostat containers, or on the base section in the vicinity thereof.

Here, "a temperature-sensitive substance" is, for example, a substance whose transparency, color or shape changes. The temperature-sensitive substance must be contained in or attached to the temperature-sensing element in such a manner as to be

measurable from the outside. Examples of the temperature-sensitive substance include inks which change color according to temperature (such as Thermoink and Thermolabel (registered trademark)), and those using shape memory alloys.

With the reagent container according to the tenth aspect of the invention, a temperature-sensing element having a temperature-sensitive substance which senses the temperature in the thermostat container and displays a visual indication of changes in the temperature is provided. Accordingly, this aspect of the invention has an advantage in that because the temperature inside the liquid-containing unit can be ascertained, the temperature inside the liquid-containing unit can be monitored, enabling highly reliable processing to be performed.

An eleventh aspect of the invention is a reagent container in which the base section comprises one or more tube fitting sections, into which a liquid-containing unit or a thermostat container can be detachably fitted. The tube fitting section may be, for example, a through hole, or may be in the form of a receptacle which accommodates the tube to be fitted. Examples of tubes include containers and instruments with a variety of functions, such as liquid-containing units, thermostat containers, measuring instruments, and pipette tips.

The reagent container according to the eleventh aspect of the invention has an advantage in that the container can be given a variety of functions by fitting removable tubes such as thermostat containers or liquid-containing units in the tube fitting section, enabling diverse and versatile processing to be performed.

A twelfth aspect of the invention is a reagent container comprising: a base section, one or more liquid-containing units for containing a reagent; a thermostat container provided so as to surround at least one of the liquid-containing units; a heating agent or a

cooling agent for heating or cooling the liquid-containing units, provided inside the thermostat container, but outside the liquid-containing unit surrounded by the thermostat container; an aperture section which is provided on the base section, and which enables gases to pass between the thermostat container and the outside; and a sealing film affixed to the top of the base section in a peelable or perforable manner which, with all or some of the liquid-containing units containing a reagent, seals the openings and the aperture sections of at least those liquid-containing units which contain a reagent.

With the reagent container according to the twelfth aspect of the invention, the openings and aperture sections of the liquid-containing units are provided at the base section, and the openings and aperture sections of at least those liquid-containing units which contain reagents are sealed by affixing a peelable or perforable sealing film. Accordingly, this aspect of the invention has an advantage in that the openings and aperture sections can be easily sealed at the base section, and the film can be removed easily and reliably when performing a process.

A thirteenth aspect of the invention is a reagent container comprising one or more liquid-containing units for containing a reagent, and a thermostat member which forms all or part of a wall of at least one of the liquid-containing units, and the thermostat member heats or cools the inside of the liquid-containing unit in accordance with an external signal.

Here, “a wall” includes not only a side wall but also a bottom wall and the like, and refers to the part surrounding the liquid-containing unit. “A thermostat member” is a member whose temperature can be raised or lowered based on an external signal.

When the thermostat member is a conductive member, the “signal” is an electromagnetic signal, that is a signal based on electricity or magnetism. It is also possible to detect the temperature of the thermostat member and generate signals based on the

temperature.

Because the thermostat member is "a thermostat member which forms all or part of a wall", the thermostat member is of approximately the same thickness as the wall of the container, or thinner. This means that if the liquid-containing unit has a thin wall, the thermostat member is also formed to be thin.

With the thirteenth aspect of the invention, thermal efficiency is high because the wall and the inside of the liquid-containing unit are in direct contact, reflection or insulation of heat by the wall can be prevented, and heat can be transmitted to the inside of the liquid-containing unit with greater efficiency than if the thermostat member were attached to the outside of the wall of the liquid-containing unit.

In addition, because the thermostat member forms the wall of the liquid-containing unit, there is no need to provide an unnecessarily large thermostat member such as a metal block on the outside of the liquid-containing unit, and all that need be provided on the outside is the drive equipment for the thermostat member, for example the battery. Consequently the overall weight of the device can be reduced.

Because the thermostat member best suited to the liquid-containing unit can be formed in advance, there is no need to provide an external thermostat member which satisfies the various requirements of the liquid-containing units or the container, which improves reactivity and versatility.

By giving the liquid-containing unit a suitable shape, the time from when the heating or cooling signal is applied until the liquid temperature reaches an even temperature distribution can be reduced, enabling processing to be performed quickly and efficiently.

Furthermore, because the thermostat member forms all or part of the wall of the liquid-containing unit, the thermostat member needs only a small heat capacity. This

enables the amount of energy required for heating or cooling to be conserved to the extent that either can be performed adequately using a battery source.

A fourteenth aspect of the invention is a reagent container in which an internal surface of the wall faces the inside of the liquid-containing unit, an external surface of the wall is outside the liquid-containing unit, and an area between the internal and external surfaces is integrally formed.

Here, "the area between the internal and external surfaces is integrally formed" means that the part of the wall sandwiched between the internal surface and the external surface of the liquid-containing unit is in the form of a solid wall composed of a metal or resin or a combination of both such that the wall cannot be separated. Accordingly, when the thermostat member which forms all or part of the wall is detachable from the wall, thermostat members which simply contact the wall, thermostat members attached in a removable manner to the wall by screws or the like, thermostat members attached in a removable manner to a separate member attached to the wall by means of welding or the like, and thermostat members which are completely separated from the wall, are precluded as they can be separated. Consequently, by forming the thermostat member to approximately the thickness required as the wall of the liquid-containing unit, the size of the reagent container and the scale of the overall device can be reduced, and the device can be used without the obtrusive presence of the heating device.

With the fourteenth aspect of the invention, because the wall is integrally formed , and the thermostat member forms all or part of the wall, the effects described above are demonstrated, thermal efficiency is further enhanced, and thermostatic control can be performed with high accuracy.

With the fourteenth aspect of the invention, the liquid-containing unit and the

reagent container can have a more compact size and a simpler construction, can be more lightweight, and can be manufactured easily and at low cost.

A fifteenth aspect of the invention is a reagent container in which the thermostat member comprises a conductive member having a predetermined electrical resistance, and the signal is an electromagnetic signal.

Here, "a predetermined electrical resistance" is a value at which a predetermined electrical current flowing inside the conductive member generates enough heat for the conductive member to reach a target temperature. In terms of surface resistivity, for example, this may be a value from several hundred ohms to several ohms per unit area, and a resistance which enables induction heating may be several ohm cms or greater, for example. The conductive member may be, for example, made of one type of substance with a predetermined electrical resistance, or of two or more types of substance with different resistances joined, fused, deposited, melted, welded, bonded, adhered or stuck together. In the case of the former, the temperature depends on the size of the current serving as the electromagnetic signal, but in the latter case the temperature depends not only on the current but also on the direction of the current because of the Peltier effect, which enables cooling as well as heating.

The "conductive member" may be a conductive substance such as a metal, a metallic compound such as metallic oxide, an alloy, a semiconductor, a metalloid, or a conductive resin, a combination of such a conductive substance with a nonconductive substance, for example ceramics, glass, or plastic, or a combination of conductive substances. For example, members formed from two different conductive substances, such as aluminum, aluminum oxide, tin oxide, iron, ferroalloys, and nichrome alloys, may be bonded, welded or joined together. Induction heating of these members can be performed

by causing a current to flow in the member, or in the case of iron or a ferroalloy, by applying a magnetic field which changes with time. In a case where a bonded product of two or more metals is used, either heating or cooling can be performed depending on the direction of the current.

Examples of the shape of the conductive member include linear, thin film, leaf, film, thin sheet, sheet, rod, and laminar shapes. For reinforcement, the conductive member may be bonded, welded, or deposited onto a nonconductive member. The "electromagnetic signal" is an electrical signal or a magnetic signal, which precludes thermodynamic signals which are based on applying heat or cold of a predetermined temperature.

The fifteenth aspect of the invention comprises a conductive member with a predetermined electrical resistance as the thermostat member. Accordingly, heating or cooling can be performed easily and reliably based on electrical or magnetic signals from an electromagnetic supply. Furthermore, the overall scale of the device can be reduced.

Moreover, according to the fifteenth aspect of the invention, the thermostat member is formed as part of the reagent container itself, and can be used in a variety of reagent containers without being bound by the shape of the reagent container provided that the positions of the contact sections match up, which enables the electromagnetic supply and the reagent container to be standardized. Furthermore, because only a small amount of material is required for the conductive member to generate heat if the resistance and the current are set to appropriate values, then the size, volume and weight of the thermostat member, and consequently the reagent container, can be reduced.

Furthermore, incidents in which only the heating equipment is driven despite a reagent container not being present can be prevented outright. Moreover a thermostatic process appropriate to each reagent container is performed, and consequently highly

reliable thermostat control can be performed.

A sixteenth aspect of the invention is a reagent container in which a contact section which receives electrical signals by contacting a terminal of an electromagnetic supply provided outside the reagent container, is provided in the reagent container.

Here, the contact section may be the conductive member itself, or may be an electrode electrically connected to the conductive member. Furthermore, the contact section may be the wall of the liquid-containing unit, or another part of the liquid-containing unit, for example a collar or flange provided at the opening facing outwards, or the base section, the base, a support plate, a support base, or a support of the reagent container. Because a contact section provides an electrical connection with the external terminal as well as supports the reagent container, in terms of construction the device can be more compact and easier to handle.

When the conductive member is a metallic member, the temperature thereof can be raised or lowered by applying or not applying lines of magnetic force, which is a magnetic signal changing with time emitted from an external electromagnetic supply. In this case, the metallic member may be made of iron or an iron alloy such as stainless steel. The temperature of the thermostat member may be changed in a dependant relationship with the change with time of the lines of magnetic force serving as the magnetic signal, and the intensity of the lines of magnetic force.

With the sixteenth aspect of the invention, because an electrical signal can be supplied through contact with the contact section, a simpler and easy to use construction can be obtained by the contact section also serving to support the reagent container. Furthermore, because thermostat control only begins once a reagent container with a predetermined construction is installed in a predetermined location and is brought into

contact with the contact section, heat generation resulting from misoperation or malfunction can be more easily prevented.

A seventeenth aspect of the invention is a reagent container in which the conductive member, forms a wall of the liquid-containing unit, covers the wall, is built into the wall, or is attached to the wall.

Here, “forms a wall of the liquid-containing unit” means that the wall itself is formed by the conductive member, “covers the wall” means that the conductive member is provided so as to cover the entire wall surface, and “is attached to the wall” means that the conductive member is provided on part of the wall surface.

With the seventeenth aspect of the invention, because the conductive member serving as the thermostat member forms the wall, covers the wall, or is built into the wall, temperature control can be performed easily by using electrical signals. Furthermore, efficiency is high because heat generation and the like are performed with the conductive member provided as the wall itself. The reagent container can also be more compact overall. Because the reagent container can be used without the heating device being obtrusive either inside or outside the reagent container, this aspect of the invention achieves ease of use.

An eighteenth aspect of the invention is a reagent container in which the wall of the liquid-containing unit comprises a frame having a gap, a slot or an aperture, and a film-shaped member or a thin plate is provided so as to cover the gap, slot or aperture in the frame.

Here, “a film-shaped member” or “a thin plate” may be made of a soft, flexible material, or a hard, non-flexible material. The “frame” is formed from a rigid substance such as resin, glass, or metal. When the frame is formed from a metallic member, the temperature of the frame can be raised or lowered by applying or not applying the lines of

magnetic force onto the frame from an external source. Furthermore, it is appropriate to form the conductive thin film serving as the thermostat member on the film-shaped member or thin plate, and use the resulting product as the wall.

With the eighteenth aspect of the invention, because covering the gap, slot or aperture in the frame with the film-shaped member or thin plate on which the thermostat member is formed, reduces the distance between the thermostat member and the inside of the liquid-containing unit, the heating or cooling effect on the contents of the liquid-containing unit is enhanced, and because the frame is provided, the liquid-containing unit is rigid.

Moreover, with the thirteenth to the eighteenth aspects of the invention, a reagent container can be formed by combining these aspects with the sixth aspect, the eighth aspect, the ninth aspect, or the eleventh aspect of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a view showing a reagent container of the invention (first embodiment), FIG. 2 is a view showing another reagent container (second embodiment), FIG. 3 is a perspective view showing a reagent container (third embodiment), FIG. 4 is diagrams showing experimental examples of heating and cooling, and FIG. 5 is a view showing another reagent container (fourth embodiment).

BEST MODE FOR CARRYING OUT THE INVENTION

With a reagent container according to the present invention, by performing heat generation and absorption primarily by means of a chemical change or chemical reaction inside a thermostat container, and by insulating external heat using the thermostat container

provided to surround the container, it is possible to reduce the electric power used for heating and cooling, or even to use electric power for temperature control only. Accordingly the overall power consumption of the device can be reduced. In addition, when the anticipated rapid improvement in battery performance, and the future commercialization of fuel cells are realized, then by incorporating these developments the present invention can provide a device capable of operating for a long time on a small amount of electric power.

Furthermore, a reagent container can be provided which is easily portable and enables a user to efficiently capture, extract, concentrate, test, and analyze genetic material such as DNA, immunogenic substances, proteins, various biological substances, microorganisms such as bacteria, and viruses.

In addition, a reagent container can be provided which enables the specification of pathogens at the site of an outbreak of a new disease, and the specification of biochemical weapons used at a battlefield or the site of a bioterrorist attack to be performed quickly and reliably *in situ*, so that the appropriate countermeasures can be taken promptly.

Specific examples of reagent containers according to the embodiments of the invention are explained below.

[Example 1]

FIG. 1 (a) is a plan view showing a reagent container 1 according to an example of the present invention, and FIG. 1 (b) and (c) are cross-sectional views taken along the lines AA and BB in FIG. 1 (a), respectively.

The reagent container 1 comprises a base section 2 in the shape of an elongated rectangle when seen from above, a plurality (10 in this example) of wells 3 corresponding to the liquid-containing units provided so as to open at the base section 2, and a single well 4

corresponding to the liquid-containing unit positioned some distance apart from the wells 3. The exterior of the well 4 is surrounded by a thermostat container 5. Accordingly, the contents of the well 4 are surrounded by a dual wall. Furthermore, an annular lid 7 is provided at the top of the thermostat container 5, which seals an opening 5a provided at the top of the thermostat container 5. The lid 7 is removable from the opening 5a. A plurality of apertures 6 for ventilation are provided in the lid 7.

Furthermore, a heating agent is contained inside the thermostat container 5 but outside the external wall that constitutes the outside surface of the well 4. The heating agent may be for example, a mixture of iron powder, activated carbon, salt, and a water-retaining substance retaining water. The amount of each substance is determined depending on the desired temperature, the reaction time, the capacity of the well 4 and the thermostat container, the material from which the well 4 is made, and the type of reagent, and the like. According to the present example, because the thermostat container 5 is positioned some distance apart from the group of wells 3, the heat of the thermostat container 5 has little effect on the wells 3, and reliable processing can be performed.

Furthermore, the present embodiment is easy to use in that the reagents held inside the wells 3 and 4 can be used by simply peeling off a film or the like (not shown) affixed to the top surface of the base section 2, while at the same time introducing air into the thermostat container 5 through the holes 6, so that heating can be achieved by the heat generated when the iron powder is oxidized.

Furthermore, in the present embodiment, because the group of wells 3 are lined up in a row in cartridge form, a single container also in cartridge form can be used to perform a series of processes, enabling processing to be performed efficiently and quickly.

[Example 2]

Next, a reagent container 10 according to a second example is described with reference to FIG. 2.

FIG. 2 (a) is a plan view showing a reagent container 10, FIG. 2 (b) and (c) are cross-sectional views taken along the lines A'-A' and B'-B' in FIG. 2 (a) respectively, FIG. 2 (d) and (e) are a plan view of a thermostat container and a cross-sectional view of the thermostat container and a well 15 serving as a liquid-containing unit surrounded by the thermostat container, and FIG. 2 (f) is a cross-sectional view taken along the line A'-A' when the thermostat container 16 is fitted to the reagent container 10.

As shown in FIG. 2 (a), the reagent container 10 according to the present example comprises a base section 11 in the shape of an elongated rectangle when seen from above, a plurality (10 in this example) of wells 12 corresponding to the liquid-containing units, provided so as to open at the base section 11, and a well 13 and a through hole 14 corresponding to the tube fitting section, both positioned some distance apart from the group of wells 12. Tubes with a variety of functions, for example liquid-containing units containing various reagents or thermostat containers or the like, can be fitted into the through hole 14.

The thermostat container 16 is formed so as to surround the outside but not the opening of a well 15 which contains a reagent, and has an inside diameter and outside diameter smaller than the well 13. A heating agent is accommodated outside the external wall that constitutes the outside surface of the well 13. An annular lid 19 is fitted to a mouth section 17a which has an annular opening at the top of the thermostat container 16, and a plurality of ventilation pores 18 through which air can enter the thermostat container 16 are provided in the lid 19. The thermostat container 16 is prevented from falling through the through hole 14 by forming the lid 19 so that the outside diameter thereof is larger than the

inside diameter of the through hole 14.

According to the present example, because the through hole 14 is positioned some distance apart from the group of wells 12, installing the thermostat container 16 in the through hole 14 has minimal effect on the other wells 12. The well 13 may hold a reagent that is hardly affected by external temperature changes, for example a suspension of magnetic particles, or may be used to perform a process that is hardly affected by external temperature changes.

Furthermore, according to the present example, because the thermostat container 16 is fitted to the through hole 14 in a removable manner, on completion of a thermostatic process the contents can be replaced by fitting a different thermostat container to continue further thermostatic processes, or various tubes with different functions can be fitted before or after the thermostatic process is performed, thereby providing for a wide variety of processing.

As follows are examples of heating agents that can be used in example 1 and example 2 as described above.

For example, 500 μl of distilled water is placed in the well 4 or the well 15, and as the heating agent, for example, 28.9 g by mass of iron powder (54% by weight), 8 g of activated carbon (15%), 1.6 g of salt (3%), and 15 g of water (28%) is used. The amount of each substance is determined according to the desired heat output and heat generation time. FIG. 4 (a) shows experimental examples of the time dependency of the temperature of the distilled water when this heating agent is used.

The reaction formula of the exothermic reaction produced by the heating agent is as follows:

$$Fe + 3/4O_2+3/2H_2O = Fe(OH)_3 + 96 \text{ kcal/mol}$$

Furthermore, in the experimental examples, in order to show that the generated temperature and the duration can be controlled by the quantity of the water-retaining substance, a water-absorbent polymer was used as the water-retaining substance, and the time dependency of the temperature of the distilled water in the well 4 or the well 15 when 0 g, 80 g, 40 g, 20 g, and 30 g of the water-absorbent polymer was added to the heating agent is shown.

According to the experimental examples, in the case where none of the water-retaining substance was included, the distilled water in the well had reached 85°C after approximately 10 minutes, the temperature began to decline after about one hour, and after two hours the temperature had returned to about room temperature. On the other hand, the examples show that by adding the various quantities of the water-retaining substance, the reaction speed, that is the temperature attained, can be controlled. This is because the heating agent is adhered and fixed onto the surface of the water-absorbent polymer, restricting the probability of the heating agent binding with oxygen. Furthermore, the reaction speed may also depend on the dispersion ratio and void ratio of the heating agent in the mixed layer.

[Example 3]

Next, a reagent container 20 according to a third example is described with reference to FIG. 3.

As shown in FIG. 3 (a), the reagent container 20 comprises a container section 21 in the shape of an elongated rectangle when seen from above, and a thermostat container 22 in the shape of a square tube which keeps some of the reagent in the container section 21 cool. The container section 21 comprises a base section 23, a plurality of wells 24 corresponding to the liquid-containing units provided so as to open at the base section 23,

and a single well 25 corresponding to the liquid-containing unit positioned a predetermined distance apart from the wells 24.

The thermostat container 22 is separate from the container section 21 to enable the thermostat container 22 to surround the well 25 serving as the liquid-containing unit, and comprises a square tube 26 which has a hollow inside whose height is equivalent to the depth of the wells 24 of the container section 21 or slightly longer, and a plurality (8 in this example) of mouth sections 27 into which the well 25 is inserted and with which the well 25 engages, formed on the top surface of the square tube 26 at intervals equivalent to the width of the base section 23 or slightly wider. The openings at both ends of the square tube 26 correspond to the apertures 29 provided in the thermostat container.

Accordingly, the reagent container 20 is assembled with a maximum of eight of the container sections 21 installed in parallel along and orthogonal to the longitudinal direction of the square tube 26. Furthermore, the inside diameter of each mouth section 27 is formed so as to closely fit the outside diameter of the well 24. As a result, leakage of cooling agent from the thermostat container 22 can be prevented, further enhancing the thermal insulating efficiency. On either one of the outside diameter of the well 24 or the inside diameter of the mouth section 27, preferably an O-ring structure is formed to improve the sealing effect between the well 24 and the mouth section 27.

Keeping the well 25 cool by means of the thermostat container 22 is achieved by, when the device is in use, spraying a liquefied cooling gas as the cooling agent from the aperture 29 in the direction of the arrow 28 in the figure. The aforementioned predetermined distance must be at least the distance from the edge of the top face of the square tube 26 of the thermostat container 22 to the nearer end of the mouth section 27, or longer.

FIG. 3 (b) shows a reagent container 30 according to another example.

The reagent container 30 comprises the container section 21 described above, and a thermostat container 31. In FIG. 3 (b), the liquid-containing unit (well) 25 of the container section 21 is engaged with the mouth section 27. The thermostat container 31 differs from the thermostat container 22 in that the hollow inside part of the square tube 26 comprises two cylindrical chambers 32 and 33 made of a heat conducting material which functions as a heat absorber, for example a metal such as copper or aluminum.

The two chambers 32 and 33 are provided with the cylinder axis direction (longitudinal direction) thereof aligned with the axial direction (longitudinal direction) of the square tube 26, so that when wells 25 are inserted in and engaged with each mouth section 27, the chambers adjoin or abut the well 25 to interpose from both sides. In this example, a liquefied cooling gas in the form of a cooling spray is sprayed into the hollow interior of the chambers 32 and 33 along the axial direction. Because in the thermostat container 31 according to this example the chambers 32 and 33 made of a heat conducting material are provided such that when assembled the chambers abut or adjoin the side face of the well 25 of the container section 21, uniform and even cooling can be achieved for the plurality of wells 25 installed in the thermostat container 31.

FIG. 4 (b) shows an experimental example relating to a cooling effect obtained in this manner.

In the experiment, 2 ml of distilled water was placed in the well 25 (made of aluminum) of the reagent container absent the thermostat container, and LPG (liquefied petroleum gas) as the liquefied cooling gas was sprayed directly onto the well 25. According to the experiment, it is apparent that the temperature reached 4°C within approximately 60 seconds, and the cooling effect was maintained to some extent.

Accordingly, it can be considered that if the thermostat container is in place when the cooling gas is sprayed directly onto the well 25, the cooling effect will persist for even longer. Here, other examples of the cooling gas include products composed of a stock solution and a propellant, which when sprayed in powder or mist form adhere to the application site in a frozen or sherbet-like state due to the evaporation heat of the propellant, thereby maintaining the cooled state. One example of such a product contains from 40.0 to 97.0 weight% of a monohydric lower alcohol and from 3.0 to 15.0 weight% of a monohydric higher alcohol as the stock solution, and dimethyl ether or liquefied petroleum gas as the propellant (Japanese Unexamined Patent Publication No. Hei 12-087017).

Moreover, the thermostat container improves thermal insulation not only for cooling but also for heating performed as described with reference to FIG. 1 and FIG. 2, by forming the combined liquid-containing unit and the thermostat member so as to be inserted and engaged into the mouth section of the thermostat member, and then inserting and engaging therein.

[Example 4]

Next, a reagent container 40 according to a fourth example is described with reference to FIG. 5.

FIG. 5 (a) is a plan view showing the reagent container 40, FIG. 5 (b) and (c) are cross-sectional views taken along the lines A"-A" and B"-B" in FIG. 5 (a) respectively, FIG. 5 (d) and (e) are a plan view of a liquid-containing unit with a thermostat member, and a cross-sectional view of a well 45 which serves as a liquid-containing unit with a thermostat member, respectively, and FIG. 5 (f) is a cross-sectional view taken along the line A"-A" when the well 45 which serves as a liquid-containing unit with a thermostat member is

installed in the reagent container 40.

As shown in FIG. 5 (a), the reagent container 40 according to the present example comprises a base section 41 in the shape of an elongated rectangle when seen from above, a plurality (10 in this example) of wells 42 corresponding to the liquid-containing units, provided so as to open at the base section 41, and a well 43 and a through hole 44 corresponding to the tube fitting section, both positioned some distance apart from the group of wells 42. Tubes with a variety of functions, for example liquid-containing units containing various reagents, can be fitted into the through hole 44.

A tin oxide film 46, which is a conductive thin film serving as the thermostatic member formed as a coating by such methods as deposition, bonding or adhesion, surrounds the outside surface but not the opening of the well 45 serving as the liquid-containing unit. A flange 49 having a radius larger than the inside diameter of the through hole 44 is provided at the annular opening of the well 45, to prevent the well 45 from falling through the through hole 44. The tin oxide film 46 serving as the conductive thin film is extended to the reverse side of the flange 49, or the reverse side of the flange 49 comprises a single contact section 49a electrically connected to the tin oxide film 46 serving as the conductive thin film, so that another contact section 46a becomes the bottom part of the tin oxide film 46. Furthermore, either the base section 41 itself or an elevated section 44a which surrounds the openings of the through hole 44 and the well 43 is formed from a conductive member. The elevated section 44a or the base section 41 is electrically connected to one of the electrodes of a battery 48, and the other electrode of the battery 48 is connected to a terminal 47. When the well 45 is installed in the through hole 44, the contact section 49a contacts the elevated section 44a or the base section 41, and the contact section 46a of the well 45 contacts the terminal 47. Thus, by simply installing the well 45 in the through hole

44, electric current can flow to the tin oxide film 46 through the terminal and the contact sections 49a and 46a, and as a result, the heat generated by the electrical resistivity of the tin oxide film 46 can heat the inside of the well 45 serving as the liquid-containing unit.

According to the present embodiment, because the through hole 44 is positioned some distance apart from the group of wells 42, installing the well 45 in the through hole 44 has minimal effect on the other wells 42. The well 43 may hold a reagent that is hardly affected by external temperature changes, for example a suspension of magnetic particles, or may be used to perform a process that is hardly affected by external temperature changes.

Furthermore, according to the present example, because the well 45 is fitted to the through hole 44 in a removable manner, on completion of a thermostatic process the contents can be replaced by fitting a different thermostat container to continue further thermostatic processes, or various tubes with different functions can be fitted before or after the thermostatic process is performed, thereby providing for a wide variety of processing.

In addition, according to the present example, a conductive thin film is used, and heating is performed by supplying current to the conductive thin film. Accordingly, because the heat capacity of the conductive thin film is small, heating can be performed without the need to supply large amounts of energy, and sufficient heating can be achieved even with a battery source. Furthermore, by using a conductive thin film in the reagent container, the weight of the container can be reduced.

FIG. 5 (g) shows a well 55 serving as the liquid-containing unit, comprising another example of a thermostat member which is able to be inserted in the through hole 44 in the base section 41 shown in FIG. 5 (a). The well 55 is formed by bonding a conductive thin film serving as a thermostat member, for example a film-like member 56a onto which a tin oxide film 56 is welded, joined or deposited, to a frame having the well 55 on its side, so

as to cover an aperture 55a. Reference numeral 59 indicates a flange.

With the well 55 according to this example, because the thermostat member contacts the liquid inside the liquid-containing unit via the film-like member or a thin plate which is comparatively thinner than the frame, heating or cooling can be performed quickly and efficiently. Furthermore, the frame gives the well 55 rigidity. In this case, a predetermined part of the tin oxide film 56 (corresponding to the single contact section described above) must contact the through hole 44 held in the base section 41 formed from a conductive member, and the terminal 47 must be positioned so as to contact another part (corresponding to the other contact section) of the tin oxide film 56 located some distance apart from the predetermined part.

In the description above, an example of a heating agent based on an oxidation reaction using iron powder was used, but this is merely an example, and depending on the desired duration and temperature, other heating agents such as those which use a hydroxylation reaction based on aluminum and lime and the like can be used. In this case, heat generation is begun by introducing water into the thermostat member through the aperture or mouth section. In addition, various exothermic reactions appropriate to the object of the test can be used. Furthermore, in the only example of a case where cooling is performed, liquefied cooling gas was used by way of a cooling spray, but the present invention is not restricted to this example, and cooling can also be performed by sealing an easily vaporized volatile alcohol or water or the like inside the thermostat container which, or a part of which (for example the lid) uses a porous substance, and then removing or perforating a sealing film which, when the device is not in use, is affixed to the part (or whole) of the thermostat container which uses the porous substance. Moreover, if a porous substance is used in the thermostat container, the porous material part which contains

numerous pores invisible to the naked eye corresponds to the aperture section.

Furthermore, by combining the cooling agent with a cold insulator inside or outside the thermostat container, the duration of the reaction can be controlled.

In addition, the temperature inside the thermostat container can be monitored by attaching to the container, on or near the thermostat container of the reaction container, a temperature-sensing element comprising a temperature sensitive substance.

Moreover, in the description of the embodiments above, 10, 11, or 5 liquid-containing units per the figure were arranged in a row in cartridge form, but the number of liquid-containing units is not restricted to these cases. Furthermore, the number of thermostat containers is not restricted to one, and a plurality of thermostat containers can be provided. In addition, the thermostat container is not restricted to those described, and the number of mouth sections is not restricted to 8, and various cases are possible including a case of one. Furthermore, regarding the arrangement of the liquid-containing units, there may be only one such unit, or there may be a plurality of liquid-containing units set in a matrix in a microplate.

In the examples above, a case was described in which a tin oxide film is used as the conductive thin film, but other metal oxides, metallic compounds, and metal substances may be used, and a film that combines not just one but two or more conductive members by bonding, deposition or welding may also be used.

Furthermore, the components, liquid-containing units, conductive thin films, thermostat containers, through holes, contact sections, terminals, wells, base sections, and the like can be combined arbitrarily while modifying appropriately to form a reagent container.

INDUSTRIAL APPLICABILITY

The present invention can be used in a variety of fields where the capture, extraction, concentration, testing, and analysis; of biological substances of humans or the like such as genetic material like DNA, immunogenic substances, proteins, and blood, of microorganisms such as bacteria, and of viruses is required. For example fields such as manufacturing, medical and health, pharmaceutical manufacturing, agriculture, fisheries, farming, biochemistry, military, and public safety.